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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/505,375	05/10/2005	Yuman Fong	08582/014002	5371

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CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

EXAMINER	
HAMA, JOANNE	

ART UNIT	PAPER NUMBER
1632	

NOTIFICATION DATE	DELIVERY MODE
05/13/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/505,375	FONG ET AL.	
	Examiner	Art Unit	
	JOANNE HAMA	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-13 and 28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-13 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 20, 2009 has been entered.

Applicant has not filed any amendment to the claims. As such, the claims filed November 2, 2007 will be considered.

Claims 1, 3-13, 14, 28 drawn to a method of treating metastasis of cancer, are under consideration.

Withdrawn Rejections

35 USC § 103

Applicant's arguments, see pages 8-11 of Applicant's response, filed February 20, 2009, with respect to the rejection of claims 1, 3-6, 8, 9, 28, as being unpatentable over Kooby et al., 1999, in view of Rodgers and McCall, 2000 have been fully considered and are persuasive. Applicant indicates that the administration of virus in Kooby is vial portal vein infusion, which is different from that of administering virus directly to the resection site. The rejection of claims 1, 3-6, 8, 9, 28 has been withdrawn.

New/Maintained Rejections

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 3-9, 28 are newly rejected under 35 U.S.C. 102(b) as being anticipated by McAuliffe et al., 2000, J. Gastrointest. Surg. 4: 580-588, as evidenced by Alemany et al., US Patent 6,403,370, patented June 11, 2002.

McAullife et al. teach clinical applications for oncolytic HSV in cancer. In the adjuvant setting, when there may be viable tumor cells present in the resection bed but the tumor cell burden is low, delivery of sufficient virus to reach MOI of 1 to 100 would be feasible. Even with no further local proliferation of virus, such high effective doses of virus will likely kill residual tumor cells. This may be an ideal setting for the use of the more attenuated G207. In the case of palliation, local virus production of progeny virus enhances the antitumor efficacy. In this situation, NV1020 would be a preferred virus (McAullife et al., page 586. 1st col., 4th parag. to 2nd col., 1st parag.).

It is noted that McAuliffe et al. indicates that local production of virus enhances antitumor efficacy. It is also noted that McAuliffe et al. do not specifically indicate the treatment of metastatic cancer. While McAuliffe et al. do not specifically indicate that the antitumor efficacy is an immune-mediated response, artisans would recognize that such is the case. Alemany et al. teach that lysis of the tumor cells generates a local tumorcidal effect. With regard to McAuliffe et al. not specifically indicating whether or not the cancer patients have metastatic cancer, an artisan would recognize that lysis of cancer cells would lead to a systemic antitumoral response that results in rejection of distant metastases, see for example Alemany et al., col. 6, 1st and 2nd parags. under Summary of the Invention, see also col. 9, line 56 to col. 10, line 13. As such, an artisan would recognize that the method is applicable to metastatic cancer patients.

With regard to the cancer being found in the lymphatic system and metastasizing to the lymph node (claims 4, 5), while McAullife et al. nor Almany et al. do not specifically teach these embodiments, it is noted that because McAuliffe et al. teach these steps, cancer in the lymphatic system would have been treated. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke 441 F.2d 660, 169 USPQ 563 (CCPA 1971). Whether the rejection is based on "inherency" under 35 USC 102, or "prima facie

obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In re Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

Thus, the claims are rejected.

Claims 1, 3-6, 8-13, 28 remain rejected under 35 U.S.C. 102(e) as being anticipated by Fong et al., US 2002/0071832 for reasons of record, December 28, 2005, July 7, 2006, February 12, 2007, July 14, 2007, January 11, 2008, August 20, 2008.

Applicant's arguments filed February 20, 2009 have been fully considered but they are not persuasive.

Applicant indicates that regarding Fong's inclusion of the mts1 promoter in a long list of promoters, Applicant disagrees that this is indicative that Fong envisioned treatment according to the presently claimed invention which requires surgical resection of a tumor, application of virus to the site of resection, and treatment of metastases at a site that is distal to the resection site. This is according to the accompanying declaration of Dr. Yuman Fong, an inventor of the instant application and US 2002/0071832. The declaration states that the passages of US 2002/0071832 are not a description of a treatment of metastases (Applicant's response, page 3). In response, while Dr. Fong indicates that the disclosure of US 2002/0071832 is not about the treatment of

metastases, nothing in US 2002/0071832 specifically indicates a limitation on the types of cancer (e.g. metastatic vs. non-metastatic) that is treated. Further, the art (see Alemany et al., above) teaches that it was known that oncolytic viruses can be used in metastatic cancer treatment because lysis of cancer cells leads to a systemic immune response. As such, an artisan would have recognized that US 2002/0071832 has applications in metastatic cancer treatment, even if Dr. Fong's declaration indicates that metastatic cancer was not the intent of US 2002/0071832.

With regard to the issue of promoters Applicant indicates that it is clear that Fong's inclusion of a list of promoters and a list of modes of administration does not meant that Fong teaches each and every combination of these promoters and routes for use in any circumstance. With regard to the route or mode of administration, wherein more specifically it is recited in the instant claims that viruses are administered to resected tumor beds, an artisan would take into account the nature of the cells at the site of the tumor bed in his/her selection of a promoter. An artisan would also note that the purpose of inoculation of virus is to ensure destruction of any tumor cells remaining at the tumor bed (Applicant's response, pages 4-6). In response, as discussed below, the art (see Alemany et al.) teaches that an artisan would administer cells to a resected tumor bed because in addition to lysing tumor cells, the lysed tumor cells induce a systemic immune response that attacks metastatic cancer. As such, an artisan would have recognized that the teachings of US 2002/0071832 is not so limited to non-metastatic cancers.

With regard to the virus being administered intravenously, Applicant indicates that that Fong mentioning the use of intravenous administration and Henderson teaching intravenous administration are not relevant to the instant claims (Applciant's response, page 6). In response, given the teaching of Alemany et al., see below, an artisan is given guidance for the administration of oncolytic virus to a resected tumor bed, as administration to the tumor bed lyses cancer cells and the lysed cancer cells induce a systemic immune response to attack metastatic tumor cells. As such, while Fong indicates in the declaration that US 2002/0071832 was not intended for treatment of metastatic cancer, an artisan would have recognized that administration of virus at the tumor bed can be used in the treatment of metastatic cancer.

Applicant indicates that claims 4, 5, 28 being drawn to treatment of lymphatic metastases, Fong does not teach the treatment of any metastases, let alone lymphatic metastases (Applicant's response, page 7). In response, the art teaches the first metastatic cancer detected in cancer patients are tumor cells that spread to lymph nodes (see Zetter Research Laboratory printout, Tumor Metastasis [online], 2004 [retrieved on 2009-05-04]. Retrieved from the Internet:< http://www.childrenshospital.org/cfapps/research/data_admin/Site229/mainpage S229P5.html>, pages 1-5, page 2, under "Lymphatic Metastasis"). As such, any patient with metastatic cancer necessarily has lymphatic metastases. Again, because Alemany et al. teach that administration to the resected tumor bed can be used to lyse cancer cells in the bed and lysed cancer cells can be used to induce a systemic immune response that can be used to treat metastatic cancer,

the method steps taught in US 2002/0071832 would have treated metastatic cancer.

Thus, the claims remain rejected.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 6, 7 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Fong et al., US 2002/0071832 in view of Wong et al., 2001, Human Gene Therapy, 12: 253-265, for reasons of record, December 28, 2005, July 7, 2006, February 12, 2007, July 24, 2007, January 11, 2008, August 20, 2008.

Applicant's arguments filed February 20, 2009 have been fully considered but they are not persuasive.

Applicant indicates that as stated above, Fong does not teach or suggest treatment of distal metastases by administration of oncolytic virus to a site of surgical resection (Applicant's response, page 8). In response, this is not persuasive, as discussed above. While Dr. Fong indicates in the declaration that there was no intention of treating metastatic tumors in US 2002/0071832, the specification of US 2002/0071832 does not specifically indicate any limitations on

the cancers that are to be treated. Further, as discussed below, the art (Alemany et al.) teaches the benefits of administering oncolytic virus to a resected tumor bed. One is that administration to the bed lyses any remaining cancer cells and the other is that lysed cancer cells induce a systemic immune response which targets metastatic cancers.

Thus, the claims remain rejected.

Claims 1, 3-13, 28 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Alemany et al., US Patent 6,403,370, patented June 11, 2002, in view of McAuliffe et al., 2000, J. Gastrointest. Surg. 4: 580-588.

Alemany et al. teach an oncolytic controlled-adenovirus (Ad) system which is generated by co-transfection of two plasmids in a helper cell line. The controlled-Ad plasmid contains one or more Ad genes regulated by a tumor-activated promoter/enhancer, the supplemental-Ad plasmid contains the remainder of the Ad genes, and the helper cell line is a tumor-derived cell line in which the tumor-activated promoter of the controlled-Ad is functional. The controlled-Ad and the supplemental-Ad complement each other in the supplemental cell line and propagate as a virus mixture. The vector mixture can be purified through a CsCl gradient and injected locally or systemically, into the tumor mass or tumor bed following surgical debulking. The tumor-activated promoter/enhancer specifically transcribes E1A and E1B that transactivate transcription and replication of the supplemental-Ad in tumor cells. Propagation of the supplemental-Ad in the tumor cells results in lysis of the tumor cells and

generates a local tumorcidal effect and a systemic antitumoral response that results in rejection of distant metastases (Alemany et al., col. 6, 1st and 2nd parags. under Summary of the Invention, see also col. 9, line 56 to col. 10, line 13). Alemany et al. teach that their viral system can also include a transgene encoding a immunomodulatory gene (Alemany et al., col. 6, lines 31-33).

While Alemany et al. teach oncolytic adenovirus, they do not teach oncolytic herpes virus.

McAuliffe et al. teach oncolytic herpes viruses, G207 and NV1020 (McAuliffe et al., abstract)..

It would have been obvious for an ordinary artisan to substitute the oncolytic adenovirus taught by Alemany et al. with that of McAuliffe et al. because both Alemany et al. and McAuliffe et al. teach oncolytic viruses and Alemany et al. teach that lysis of tumor cells trigger a tumorcidal effect and a systemic antitumoral response that results in rejection of distant metastases.

Thus, the claims are rejected.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Mondays, Tuesdays, Thursdays, and Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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/Joanne Hama/
Primary Examiner
Art Unit 1632